wherein:

a1

n is the number of different molecules in the sample;

N_i is the number of i^{th} molecules in the sample; and

M_i is the mass of the i^{th} molecule.

a2

7. (Amended) The mixture according to Claim 1, wherein the oligomer is covalently coupled to Lys^{B29} of the human insulin drug.

a3

10. (Amended) The mixture according to Claim 1, wherein the human insulin-drug oligomer has an increased resistance to degradation by chymotrypsin when compared to the resistance to degradation by chymotrypsin of a polydispersed mixture of insulin drug-oligomer conjugates having the same number average molecular weight as the mixture.

16. (Amended) A mixture of conjugates, each comprising insulin coupled to an oligomer that comprises a polyethylene glycol moiety, wherein the mixture has a dispersity coefficient (DC) greater than 10,000, where

$$DC = \frac{\left(\sum_{i=1}^{n} N_i M_i\right)^2}{\sum_{i=1}^{n} N_i M_i^2 \sum_{i=1}^{n} N_i - \left(\sum_{i=1}^{n} N_i M_i\right)^2}$$

a4

wherein:

n is the number of different molecules in the sample;

N_i is the number of i^{th} molecules in the sample; and

M_i is the mass of the i^{th} molecule; and

wherein the conjugate comprises a first oligomer and a second oligomer; and

wherein the first oligomer is covalently coupled at Lys^{B29} of the insulin and the second oligomer is covalently coupled at N-terminal A1 or N-terminal B1 of the insulin.

17. (Amended) The mixture according to Claim 1, wherein the human insulin drug is covalently coupled to the oligomer.

18. (Amended) The mixture according to Claim 16, wherein the insulin is covalently coupled to at least one of the oligomers by a hydrolyzable bond.

19. (Amended) The mixture according to Claim 16, wherein the insulin is covalently coupled to the polyethylene glycol moiety of at least one of the oligomers.

a4

20. (Amended) The mixture according to Claim 16, wherein at least one of the oligomers comprises a lipophilic moiety covalently coupled to the polyethylene glycol moiety.

21. (Amended) The mixture according to Claim 16, wherein at least one of the oligomers comprises a lipophilic moiety.

22. (Amended) The mixture according to Claim 21, wherein the insulin is covalently coupled to the lipophilic moiety.

25. (Amended) The mixture according to Claim 16, wherein the first and the second oligomers are the same.

a5

26. (Amended) The mixture according to Claim 16, wherein at least one of the oligomers comprises a first polyethylene glycol moiety covalently coupled to the insulin by a non-hydrolyzable bond and a second polyethylene glycol moiety covalently coupled to the first polyethylene glycol moiety by a hydrolyzable bond.

27. (Amended) The mixture according to Claim 26, wherein the oligomer(s) comprising a first polyethylene glycol moiety covalently coupled to the insulin by a non-hydrolyzable bond and a second polyethylene glycol moiety covalently coupled to the first polyethylene glycol moiety by a hydrolyzable bond further comprise a lipophilic moiety covalently coupled to the second polyethylene glycol moiety.

a5

28. (Amended) The mixture according to Claim 16, wherein each of the conjugates is amphiphilically balanced such that each conjugate is aqueously soluble and able to penetrate biological membranes.

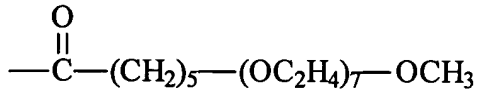
30. (Amended) A method of treating insulin deficiency in a subject in need of such treatment, said method comprising:

a6

administering an effective amount of the composition of claim 1 to the subject to treat the insulin deficiency.

46. (Amended) A mixture of conjugates, each comprising an insulin drug coupled to an oligomer that comprises a polyethylene glycol moiety, said mixture having a molecular weight distribution with a standard deviation of less than about 22 Daltons, wherein the insulin drug is human insulin, and the oligomer is covalently coupled to Lys^{B29} of the human insulin and has the formula:

a7



50. (Amended) A mixture of conjugates, each comprising an insulin drug coupled to an oligomer that comprises a polyethylene glycol moiety,

a8

wherein each polyethylene glycol moiety has the same number of polyethylene glycol subunits,

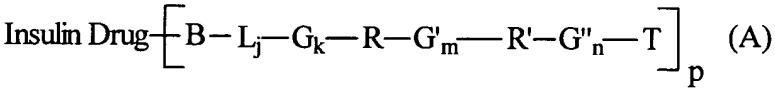
wherein each oligomer is covalently coupled to Lys^{B29} of the human insulin and has the formula:

a8

; and

wherein the mixture has a molecular weight distribution with a standard deviation of less than about 22 Daltons.

52. (Amended) A mixture of conjugates in which each conjugate is the same and has the formula:



(A)

wherein:

B is carbonyl;

L is a linker moiety;

a9

G, G' and G" are individually selected spacer moieties;

R is C_5 alkylene and R' is polyethylene glycol having 7 polyethylene glycol subunits;

T is methoxy;

j is 0 or 1;

k, m and n are 0; and

p is an integer from 1 to the number of nucleophilic residues on the insulin drug.

Please add the following new claims:

68. (New) The mixture according to claim 16, wherein at least one of the oligomers comprises a polyethylene glycol moiety having at least 2 polyethylene glycol subunits.

a10

69. (New) The mixture according to claim 16, wherein at least one of the oligomers comprises a polyethylene glycol moiety having at least 5 polyethylene glycol subunits.